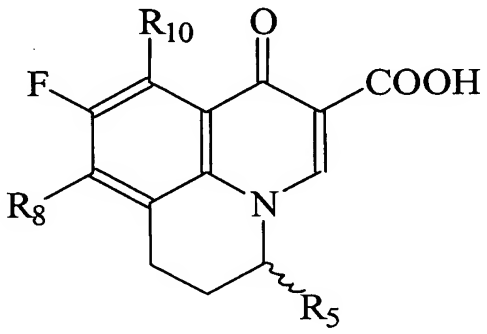
IN THE CLAIMS

1. (Original) A stable pharmaceutical composition comprising:

a pharmaceutically effective amount of benzoquinolizine-2-carboxylic acid antimicrobial drug of the formula:



(I)

wherein:

R_5 is C_{1-6} alkyl, as a mixture of enantiomers or in a stereochemical orientation;

R_8 is 4-hydroxypiperidinyl optionally further substituted with one or more C_{1-6} alkyl, hydroxypiperidinyl optionally further mono/poly substituted with C_{1-6} alkyl;

R_{10} is selected from H, C_{1-5} alkyl, amino, alkylamino and acylamino groups;

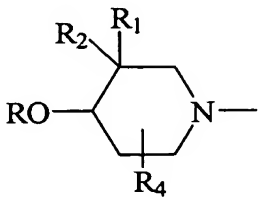
or an optical isomer, diastereomer or enantiomer thereof, or polymorphs and pseudopolymorphs or prodrugs thereof or pharmaceutically acceptable salts and hydrates thereof or mixtures thereof; singly or in combination with

a pharmaceutically effective amount(s) of a retinoid, an antibacterial, a steroid/non-steroid antiinflammatory agent, an antifungal agent or mixtures thereof.

2. (Original) The composition of claim 1 wherein in the formula (I),

R_5 is CH_3, in S-orientation.

R_8 is



(II)

wherein:

R is hydrogen, C_1-C_6 alkyl, glycosyl, aralkyl, C_1-C_6 alkanoyl , or aminoalkanoyl or R is $C_6H_{11}O_6$, PO_3H_2 or SO_3H thus giving respectively the gluconic acid, phosphoric acid and sulfonic acid ester derivatives of the compounds;

R_1 and R_2 are the same or different and represent H, C_{1-4} alkyl, aralkyl, aminoalkyl, trifluoroalkyl or halogen;

R_4 is H, C_{1-4} alkyl, CF_3, phenyl, or F; R_4 is present at one or more of the positions of 2-, 4-, 5-, or 6- of the piperidine ring; and

R_{10} is selected from H, C_{1-5} alkyl, amino, alkylamino or acylamino groups.

3. (Original) The composition of claim 1, wherein the benzoquinolizine-2-carboxylic acid antimicrobial drug is selected from the group consisting of

RS-(±)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo [i,j]quinolizine-2-carboxylic acid;

R(+)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo [i,j]quinolizine-2-carboxylic acid;

S-(-)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo [i,j]quinolizine-2-carboxylic acid;

RS-(±)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo [i,j]quinolizine-2-carboxylic acid arginine salt and solvatomorphic or polymorphic forms thereof;

R(+)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo [i,j]quinolizine-2-carboxylic acid arginine salt and solvatomorphic or polymorphic forms thereof;

S-(-)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo [i,j]quinolizine-2-carboxylic acid arginine salt and solvatomorphic or polymorphic forms thereof;

RS-(±)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo [i,j]quinolizine-2-carboxylic acid 0.2 hydrate;

R(+)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-

1H,5H-benzo [i,j]quinolizine-2-carboxylic acid 0.2 hydrate;

S-(-)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo [i,j]quinolizine-2-carboxylic acid 0.2 hydrate;

S-(-)-9-fluoro-6,7-dihydro-8-{trans-4-(RS)-hydroxy-3-(RS)-methylpiperidin-1-yl}-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid;

S-(-)-9-fluoro-6,7-dihydro-8-{cis-4-(RS)-hydroxy-3-(RS)-methylpiperidin-1-yl-5-methyl-oxo-1H,5H-benzo[i, j]quinolizine-2-carboxylic acid;

S-(-)-9-fluoro-6,7-dihydro-8-{cis-(-)-4-R-hydroxy-3-S-methylpiperidin-1-yl}-5-methyl-1-oxo-1H,5H-benzo[i, j]quinolizine-2-carboxylic acid;

S-(-)-9-fluoro-6,7-dihydro-8-{cis-(+)-4-S-hydroxy-3-R-methylpiperidin-1-yl}-5-methyl-1-oxo-1H,5H-benzo[i, j]quinolizine-2-carboxylic acid; and

S-(-)-9-fluoro-6,7-dihydro-8-(3-ethyl-4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid (mixture of cis racemate and trans racemate) and pure stereoisomers thereof.

4. (Original) The composition of claim 3, wherein the benzoquinolizine-2-carboxylic acid antimicrobial drug is S-(-)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid arginine salt and solvatomorphic or polymorphic forms thereof.

5. (Original) The composition of claim 3, wherein the benzoquinolizine-2-carboxylic acid antimicrobial drug is S-(-)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid 0.2 hydrate.

6. (Original) The composition of claim 3, wherein the benzoquinolizine-2-carboxylic acid antimicrobial drug is S-(-)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid.

7. (Original) The composition of claim 1, wherein the benzoquinolizine-2-carboxylic acid antimicrobial drug comprises about 0.1 – 10 % by weight of the composition.

8. (Original) The composition of claim 1, wherein the benzoquinolizine-2-carboxylic acid antimicrobial drug comprises about 1 % by weight of the composition.

9. (Original) The method of claim 1, wherein the benzoquinolizine-2-carboxylic acid antimicrobial drug comprises about 0.5 % by weight of the composition.

10. (Original) The composition of claim 1, wherein said retinoid is selected from the group consisting essentially of benzoyl peroxide, dichloroacetic acid, glutaraldehyde, resorcinol, retinoic acid, salicylic acid, adapalene, algestone acetophenide, azelaic acid, benzoyl peroxide, cioteronel, cyproterone, isotretinoin, motretinide, tretinoin, tazarotene, tioxolone, combinations and mixtures thereof.

11. (Original) The composition of claim 9, wherein the retinoid comprises adapalene.

12. (Original) The composition of claim 1, wherein said antibacterial is selected from the classes of aminoglycosides, cephalosporins, diaminopyridines, oxazolidinones, sulfonamides, tetracyclines or combinations of these classes.

13. (Original) The composition of claim 1, wherein said steroid is selected from the group consisting essentially of 21-acetoxypregnnolone, alclometasone, algestone, amcinonide, beclomethasone, betamethasone, budesonide, chloroprednisone, ciclesonide, clobetasol, clobetasone, clocortolone, cloprednol, corticosterone, cortisone, cortivazol, deflazacort, desonide, desoximetasone, dexamethasone, diflorasone, diflucortolone, difluprednate, enoxolone, fluazacort, flucloronide, flumethasone, flunisolide, fluocinolone acetonide, fluocinonide, fluocortin butyl, fluocortolone, fluorometholone, fluperolone acetate, fluprednidene acetate, fluprednidene acetate, fluprednisolone, flurandrenolide, fluticasone propionate, formocortal, halcinonide, halobetasol propionate, halometasone, halopredone acetate, hydrocortamate, hydrocortisone, loteprednol etabonate, mazipredone, medrysone, meprednisone, methylprednisolone, mometasone furoate, paramethasone, prednicarbate, prednisolone, prednisolone 21-diethylaminoacetate, prednisolone sodium phosphate, predisone, prednival, prednylidene,

pimexolone, tixocortol, triamcinolone, triamcinoloneacetonide, triamcinolone benetonide, triamcinolone hexacetonide, combinations and mixtures thereof.

14. (Original) The composition of claim 13, wherein the steroid comprises clobetasol.

15. (Original) The composition of claim 13, wherein the steroid comprises mometasone.

16. (Original) The composition of claim 1, wherein said non-steroid antiinflammatory agent is selected from the group consisting essentially of ibuprofen, indomethacin, ketoprofen, flurbiprofen, celecoxib, valdecoxib, rofecoxib, varecoxib, parecoxib, meloxicam, nimesulide, etodolac, combinations and mixtures thereof.

17. (Original) The composition of claim 1, wherein said antifungal agent is selected from the classes of polyenes, allylamines, imidazoles, thiocarbamates, triazoles or combinations of these classes.

18. (Original) The composition of claim 1, wherein said antifungal agent is selected from amphotericin, nystatin, caspofungin, griseofulvin, oligomycins, butenafine, naftifine, terbinafine, bifonazole, clotrimazole, ketoconazole, miconazole, liranaftate, tolnaftate, fluconazole, itraconazole, or voriconazole.

19. (Original) The composition of claim 18, wherein the antifungal agent comprises butenafine.

20. (Original) The composition of claim 1, wherein the pharmaceutically acceptable vehicle further comprises a pH modifying agent selected from acids, bases, inorganic basic salts, organic basic salts, buffering agents or mixtures thereof.

21. (Original) The composition of claim 1, that is in a physical form selected from drops, pastes, ointments, creams, milks, pomades, powders, impregnated pads, tulles, solutions, gels, shampoos, lotions, suspensions, microspheres, nanospheres, lipidic vesicles,

polymeric vesicles, polymeric patches or biological inserts.

22. (Original) A method of treating and/or preventing a bacterial infection disease comprising:

administering to a subject in need thereof, a pharmaceutical composition comprising:

a pharmaceutically effective amount of benzoquinolizine-2-carboxylic acid antimicrobial drug of the formula (I) according to claim 1; singly or in combination with a pharmaceutically effective amount(s) of a retinoid, an antibacterial, a steroid/non-steroid antiinflammatory agent, an antifungal agent or mixtures thereof.

23. (presently amended) The method of claim ~~33~~ 22, wherein the benzoquinolizine-2-carboxylic acid antimicrobial drug is RS-(±)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid arginine salt and solvatomorphic or polymorphic forms thereof.

24. (Original) The method of claim 33, wherein the benzoquinolizine-2-carboxylic acid antimicrobial drug is S-(-)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid arginine salt and solvatomorphic or polymorphic forms thereof.

25. (Original) The method of claim 33, wherein the benzoquinolizine-2-carboxylic acid antimicrobial drug is S-(-)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid 0.2 hydrate.

26. (Original) The method of claim 33, wherein the benzoquinolizine-2-carboxylic acid antimicrobial drug is S-(-)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid.

27. (Original) The method of claim 33, wherein the benzoquinolizine-2-carboxylic acid antimicrobial drug comprises about 0.1 – 10 % by weight of the composition.

28. (Original) The method of claim 33, wherein the benzoquinolizine-2-carboxylic acid antimicrobial drug comprises about 1 % by weight of the composition.

29. (Original) The method of claim 33, wherein the benzoquinolizine-2-carboxylic acid antimicrobial drug comprises about 0.5 % by weight of the composition.

30. (Original) The method of claim 33, wherein the retinoid comprises adapalene.

31. (Original) The method of claim 33, wherein said antibacterial is selected from the classes of aminoglycosides, cephalosporins, diaminopyridines, oxazolidinones, sulfonamides, tetracyclines or combinations of these classes.

32. (Original) The method of claim 33, wherein the steroid comprises clobetasol.

33. (Original) The method of claim 33, wherein said non-steroid antiinflammatory agent is selected from the group consisting essentially of ibuprofen, indomethacin, ketoprofen, flurbiprofen, celecoxib, valdecoxib, rofecoxib, varecoxib, parecoxib, meloxicam, nimesulide, etodolac, combinations and mixtures thereof.

34. (Original) The method of claim 33, wherein the antifungal agent comprises butenafine.

35. (Original) The method of claim 33, wherein said composition is in a physical form selected from concentrates, drops, pastes, ointments, creams, milks, pomades, powders, impregnated pads, tulles, solutions, gels, sprays, shampoos, lotions, suspensions, microspheres, nanospheres, lipidic vesicles, polymeric vesicles, polymeric patches or biological inserts.

36. (Original) The method of claim 33, wherein the subject is an animal or human.

37. (Original) The method of claim 33, wherein the route of administration is selected

from ocular, nasal, otic, rectal, vaginal, intradermal, intratumoral, intralesional, intravascular, topical, transdermal, local, regional, or loco-regional.

Respectfully submitted,

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